Matched Unrelated vs. Haploidentical donor for allogeneic stem cell transplantation in patients with Acute Leukemia with identical GVHD prophylaxis - A randomized porspective European trial.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON52639

Source
ToetsingOnline

Brief title
HaploMUD study

Condition

- Leukaemias
- Leukaemias

Synonym
Acute leukemia; high risk MDS

Research involving
Human

Sponsors and support

Primary sponsor: University Medical Center Hamburg-Eppendorf
Source(s) of monetary or material Support: University Medical Center Hamburg-Eppendorf

Intervention

Keyword: acute leukemia, allogeneic stem cell transplantation, haploidentical donor, matched unrelated donor

Outcome measures

Primary outcome

- Relapse incidence at two years between both arms.

Secondary outcome

- Overall survival at two years between both arms

- Overall survival for all patients assigned to one of the two treatment arms

as time to event endpoint

- Comparison of GVHD/relapse-free survival as composite endpoint in both arms

- Comparison of non-relapsed mortality (NRM) at 1 and 2 years after allogeneic

SCT in both arms

- Comparison of acute graft-versus-host disease (aGVHD) on day +100 and 1 year

(max grade) after allogeneic SCT between both arms

- Comparison of chronic graft-versus-host disease (cGVHD) at 1 and 2 years

after allogeneic SCT between both arms

- Comparison of toxicity of both regimens between both arms

- Comparison of immune reconstitution and full donor chimerism between both

arms

- Evaluation of Sorror Risk Score on outcome after allogeneic SCT

- Comparison of QOL (FACT-BMT) before and after transplantation at day +100, 6

m, 1 year,2 years between both arms

Study description

Background summary

Allogeneic stem cell transplant for acute myeloid leukemia and high risk MDS from a matched unrelated donor (10/10 HLA) has been regarded as the best alternative donor option if no HLA-identical sibling is available. The use of post-transplant cyclophosphamide as GVHD prophylaxis has increased the number of haploidentical donor cell transplantations worldwide, and retrospective studies suggest similar outcome and a trend for lower relapse if myeloablative conditioning is used. If the outcome of haploidentical stem cell transplantation is improved by a lower rate of relapse, this will have major input in the field of stem cell transplantation resulting in a faster donor availability and in cost reduction of the stem cell procedure. Thus, it is important to perform a randomized prospective trial with identical conditioning regimen and identical GVHD prophylaxis with post-transplantation cyclophosphamide

Hypothesis: haploidentical stem cell transplantation with post cyclophosphamide induces a stronger anti-leukemic activity in comparison to 10/10 HLA matched unrelated donor and reduces the risk of relapse at 2 years after stem cell transplantation by 10%.

Study objective

Primary objective of this open label, two-arm, multicenter, multinational, randomized trial is to compare anit-leukemic activity of allogeneic stem cell transplantation for patients with acute leukemia in complete remission between a 10/10 HLA matched unrelated donor and a haploidentical donor.

Secondary objectives are to assess and compare the safety and efficacy of study treatments therapy in both study arms on non-relapse mortality (NRM), relapse-free survival (RFS), overal survival (OS), QOL, toxicity, development of acute and chronic GvHD as well as engraftment and chimerism and impact of measurable residual disease.

Study design

Open label, two-arm, mulicenter, multinational, randomized phase II trial. Treatment arm A is allogeneic stem cell transplantation form 10/10 HLA matched unrelated donor. Treatment arm B is allogeneic stem cell transplantation from haploidentical donor.

Intervention

Allogeneic stem cell transplantation with PBSC as stem cell source from the matched unrelated donor or haploindentical donor.

The conditioning regime in both arms is the same, but based on patients age:
<= 50 years: Busulfan (16 mg/kgBW orally or 12.8 mg/kgBW i.v.) / fludarabine (160 mg/m2) or TBI (12 - 13.2 Gy) / fludarabine (160 mg/m2)
> 50 years (or Sorror score >= 3): Busulfan (12 mg/kgBW orally or 9.6 mg/kgBW i.v.) / fludarabine (160 mg/m2) or TBI (8 Gy) / fludarabine (160 mg/m2)

The Graft versus Host Disease prophylaxe is the same in both arms:
Cyclophosphamide 50 mg/kg on day +3 and +4
Tacrolimus from day +5 until day +120
MMF from day +5 until day +35

Study burden and risks

the risk associated with paritcipation is the same as the regular risks of undergoing an allogeneic stemcell transplantation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- AML intermediate or high risk according to ELN or ALL high risk according to ESMO guidelines in 1. CR or AML/ALL in 2. CR, or high risk MDS (according to IPSS-R) in 1. CR or 2. CR.
- Patients age 18 - 70 years.
- Signed informed consent form
- ECOG <= 2
- 10/10 HLA-matched unrelated donor and haploidentical (>= 5/10 and <= 8/10 HLA) relative
matched donor

Exclusion criteria

- Severe renal, hepatic, pulmonary or cardiac disease,
- Positive serology for HIV
- Pregnant or lactating women
- Uncontrolled invasive fungal infection at time of screening (baseline)
- Serious psychiatric or psychological disorders
- Uncontrolled severe autoimmune disease or uncontrolled other malignancy
- Availability of an HLA-identical sibling as donor source

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-12-2023
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	08-04-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04232241
CCMO	NL72936.000.21

Study results

Date completed: 13-12-2024

Actual enrolment: 3

Summary results
Trial ended prematurely